



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/057,108

01/25/2002

Geert Plaetinck

D00590.70011.US

1549

23628 7590 06/22/2009
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER

SHIN, DANA H

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

06/22/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/057,108	Applicant(s) PLAETINCK ET AL.	
	Examiner DANA SHIN	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13,17-22,25-27 and 54-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13,17-22,25-27 and 54-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4-21-2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on April 21, 2009.

Currently, claims 13, 17-22, 25-27, and 54-56 are pending and under examination on the merits in the instant case.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Response to Arguments

Applicant's arguments and the declaration under 37 CFR 1.132 filed on April 21, 2009 with respect to claims 13, 17-22, 25-27, and 54-56 have been considered but are moot in view of the new ground(s) of rejection. See below.

In addition, it is noted that the declaration is incomplete because the alleged expertise of the declarant is not adequately supported by curriculum vitae, which was allegedly attached as "Exhibit 1".

Maintained Rejections

Claim Rejections - 35 USC § 102

Claim 20 remains rejected under 35 U.S.C. 102(a) as being anticipated by Fire et al. (WO 99/32619 A1) for the reasons of record as set forth in the Office action mailed on October 27, 2008 and for the reasons stated below.

Applicant's arguments filed on April 21, 2009 have been fully considered but they are not persuasive. Applicant argues that since claim 20 depends from claims 13 and 19 that are not rejected, claim 20 must be novel and patentable over Fire et al. Applicant's attention is directed to the fact that the effective filing date for claim 20 differs from that for claims 13 and 19 for the reasons of record (see for example page 3 of the last Office action), and therefore, the Fire et al. WO document qualifies as prior art under 35 U.S.C. 102(a) only for claim 20, not claims 13 and 19. Since applicant's argument is not persuasive, this rejection is maintained.

Claim 20 remains rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al. (US 6,506,559 B1) for the reasons of record as set forth in the Office action mailed on October 27, 2008 and for the reasons stated below.

Applicant's arguments filed on April 21, 2009 have been fully considered but they are not persuasive. Applicant argues that since claim 20 depends from claims 13 and 19 that are not rejected, claim 20 must be novel and patentable over Fire et al. Applicant's attention is directed to the fact that the effective filing date for claim 20 differs from that for claims 13 and 19 for the reasons of record (see for example page 3 of the last Office action), and therefore, the Fire et al.

Art Unit: 1635

U.S. Patent qualifies as prior art under 35 U.S.C. 102(e) only for claim 20, not claims 13 and 19.

Since applicant's argument is not persuasive, this rejection is maintained.

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 20 is rejected under 35 U.S.C. 102(a) as being anticipated by Timmons et al.

(*Nature*, 1998, 395:854, citation of record).

The claim is drawn to a method for down-regulating gene expression in *C. elegans* by feeding a micro-organism that comprises an expression vector comprising two T7 promoters flanking the gene that produces a dsRNA that down-regulates gene expression in the *C. elegans*.

Note that neither of the GB priority documents provides adequate support for the claimed “T7, T3 and SP6 promoter(s)” limitation specifically recited in claim 20. Hence, the priority is granted only insofar as the filing date of 09/347,311, which is July 2, 1999.

Timmons et al. teach that one can down-regulate gene expression in *C. elegans* by feeding *E. coli* comprising a vector comprising two T7 promoters that flank the gene, wherein the vector expresses the gene, which is a dsRNA that down-regulates targeted gene expression in *C. elegans*. See the left column: "We find that *Escherichia coli* bacteria expressing dsRNAs can

Art Unit: 1635

confer specific interference effects on the nematode larvae that feed on them." See the entire reference including Figure 1. Accordingly, all claim limitations are taught by Timmons et al.

Claims 13, 18, 21, 25, and 55 are rejected under 35 U.S.C. 102(a) as being anticipated by Timmons et al. (*East Coast Worm Meeting Abstract 180*, May 12, 1998, applicant's citation).

The claims are drawn to a method for down-regulating target gene expression in *C. elegans* comprising feeding bacterium to *C. elegans*, wherein the bacterium comprises an expression vector comprising a promoter flanking a DNA sequence that is transcribed by the promoter, wherein the DNA is produced as a dsRNA, wherein the promoter is a tissue-specific promoter.

Timmons et al. teach that one can feed *C. elegans* with bacteria that express dsRNA such as GFP dsRNA or unc22 dsRNA, wherein the dsRNA is expressed from a muscle tissue specific promoter myo3 and the dsRNA down-regulates target gene expression/activity in the bacteria-fed *C. elegans*. Since the bacteria comprising a "myo3:dsRNA" construct successfully transcribes and thereby expresses the dsRNA in the bacteria-fed *C. elegans*, and since Timmons et al. perform the active steps of the claimed methods, it inherently and logically flows that the bacteria organism fed to *C. elegans* must be adapted to express a transcription factor that participates in transcribing or expressing the promoter-flanked dsRNA such as GFP dsRNA or unc22 dsRNA, absent evidence to the contrary. Accordingly, all claim limitations are taught by Timmons et al.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 13, 17-22, 25-27, and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Timmons et al. (*East Coast Worm Meeting Abstract 180*, May 12, 1998, applicant's citation) in view of Raftery et al. (*Diagnostic Molecular Pathology: The American Journal of Surgical Pathology*, 1993, 2:120-124), Wang et al. (*Gene*, 1991, 100:195-199), Vanfleteren (*Experientia*, 1976, 32:1087-1088), and Talkad et al. (*Journal of Bacteriology*, 1978, 135:528-541, citation of record).

The claims are drawn to a method for down-regulating target gene expression in *C. elegans* comprising feeding a micro-organism to *C. elegans*, wherein the micro-organism comprises an expression vector comprising a promoter or promoters flanking a DNA sequence that is transcribed by the promoter(s), wherein the DNA is produced as a dsRNA, and the promoter or promoters are T7 or T3, wherein the micro-organism is *E. coli* bacterium or a yeast cell, wherein the *E. coli* is a RNase III negative strain.

Timmons et al. teach that one can feed *C. elegans* with bacteria that express dsRNA such as GFP dsRNA or unc22 dsRNA, wherein the dsRNA is expressed from a muscle tissue specific promoter myo3 and the dsRNA down-regulates target gene expression/activity in the bacteria-fed *C. elegans*. Thus, Timmons et al. teach a method of down-regulating target expression/activity in *C. elegans* by feeding bacteria comprising a single promoter-flanked dsRNA "myo3:GFP dsRNA" or "myo3:unc22 dsRNA" construct, each of which transcribes and

Art Unit: 1635

expresses GFP dsRNA and unc 22 RNA in the bacteria-fed *C. elegans* but do not teach feeding bacteria comprising a construct comprising two promoters-flanked dsRNA.

Raftery et al. teach that one can construct an expression vector that produces two complementary RNA strands (dsRNA) by flanking the desired DNA sequence of the antisense and sense strands with two opposing promoters: T7 RNA polymerase promoter at the 5' and SP6 RNA polymerase promoter at the 3'. See the entire reference including Figure 2.

Wang et al. teach a gene expression vector structure comprising two bidirectional promoters, a 5' T7 promoter and a 3' T3 promoter, which flank a multiple cloning site for inserting a desired DNA sequence for expression. They teach that the gene expression vector comprising two promoters efficiently transcribes and expressed the inserted DNA/gene sequence encoding a protein when expressed in *E. coli*.

Vanfleteren teaches that one can inexpensively and effectively cultivate or grow *C. elegans* on a large scale for research purpose by feeding inexpensive yeast extract.

Talkad et al. teach RNase III-deficient *E. coli* strains. They teach that RNase III cleaves double-stranded RNAs.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Timmons et al. by replacing the single promoter-driven dsRNA expression vector with an expression vector comprising two bi-directional RNA polymerase promoters selected from T7, T3, and SP6, each expressing the sense or antisense strand of the dsRNA as taught by Raftery et al. and Wang et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because feeding bacteria comprising single promoter-driven dsRNA to *C.*

Art Unit: 1635

C. elegans with a resultant effect of down-regulating target expression/activity in the bacteria-fed *C. elegans* was an art-recognized methodology for RNAi-mediated down-regulation of target expression/activity in *C. elegans*, and because two different options for producing double-stranded RNA molecules by either one promoter or two opposing, bi-directional promoters selected from a tissue-specific promoter, T7 promoter, T3 promoter, and SP6 promoter in an expression vector were known in the art as taught by Timmons et al., Raftery et al., and Wang et al. Further, since the food source for feeding *C. elegans* was known to include both *E. coli* bacteria and yeast as taught by Vanfletern, one of ordinary skill in the art would have been motivated to feed either *E. coli* bacteria or yeast comprising an expression vector that produces a dsRNA by two bi-directional promoters in order to down-regulate target expression/activity by RNAi mechanism in *C. elegans*. Further, since the RNAi-inducing dsRNA was known to be cleaved by RNase III and since *E. coli* strain lacking RNase III was available in the art as taught by Talkad et al., one of ordinary skill in the art would have been motivated to utilize an RNase III-deficient *E. coli* bacterium to transform it to contain an expression vector comprising a dsRNA flanked by two promoters, wherein the dsRNA cannot be cleaved inside the RNase III-deficient *E. coli*, thereby allowing the dsRNA to be successfully expressed in the *C. elegans* that digested the RNase III-deficient *E. coli*. Since the skills to modify the method of Timmons et al. to comprise two bi-directional promoters to synthesize and express double-stranded RNA inside *C. elegans* fed on *E. coli* or yeast were within the technical grasp of one of ordinary skill in the art at the time the invention was made, the claims taken as a whole would have been *prima facie* obvious at the time of filing.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Art Unit: 1635

Claims 13, 17-22, 25-26, and 54-56 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-16 and 20-22 of U.S. Patent No. 7,005,423 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a method for expressing a dsRNA in *C. elegans* by feeding a bacterium, *E. coli* or yeast cells comprising two promoters selected from T7, T3, SP6, or a tissue-specific myo3 promoter. As such, the claims in the instant application and the issued patent are overlapping in scope and are obvious variants of each other.

Claims 13, 17-22, 25-26, and 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 41-46 of copending Application No. 12/055,607. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a method for down-regulating target expression with a dsRNA in *C. elegans* by feeding a bacterium *E. coli* comprising two promoters. Further, the specification of 12/055,607 teaches that the two promoters are selected from T7, T3, SP6 promoters. See paragraphs 0019As such, the claims in the instant application and the issued patent are overlapping in scope and are obvious variants of each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635